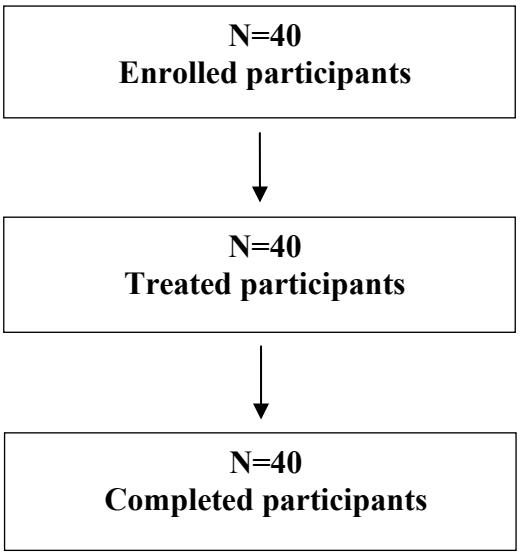
Participant flow



Baseline characteristics

Demographic data		Safety and PK set N=40
Sex	Male – n (%)	22 (55.0%)
	Female – n (%)	18 (45.0%)
Smoking History	Smokers – n (%)	25 (62.5)
	Non-smokers or past smokers – n (%)	15 (37.5)
Cannabis use frequency	Once during the past 3 months – n (%)	25 (62.5)
	Once a month – n (%)	10 (25.0)
	Twice a month – n (%)	4 (10.0)
	Once a week – n (%)	1 (2.5)
Age (years)	Mean ± SD	33.2±9.7
Body weight (kg)	Mean ± SD	69.55±12.60
Height (cm)	Mean ± SD	170.9±9.4
BMI (kg/m^2)	Mean ± SD	23.70±3.14

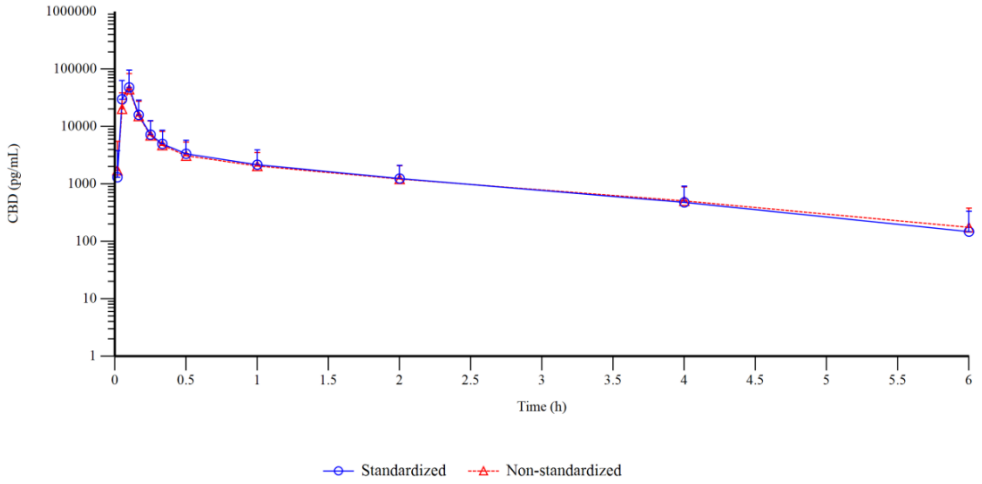
Number and percentage - n (%) - of participants are shown for qualitative measures; mean ± standard deviation (SD) are shown for quantitative measures

Outcome measures

Pharmacokinetics (PK) results

Primary PK endpoint:

CBD plasma concentration-time profiles following the standardized and non-standardized product use are presented in the figure below (logarithmic/linear scale):



CBD PK parameters are summarised by descriptive statistics in the following table:

PK parameter (Unit)	**CBD PK parameters**	
	Standardized Use N=40	**Non-standardized use N=40**
C_{max} (pg/mL)	31110.821 (164.755)	29712.938 (161.594)
T_{max} (h)	0.1 (0.05-0.167)	0.1 (0.05-0.102)
AUC_{0-t} (h*pg/mL)	8129.446 (176.28)	7668.044 (178.704)
AUC_{0-6} (h*pg/mL)	8404.369 (161.329)	8003.592 (164.191)
AUC_{0-inf} (h*pg/mL)	11254.087 (84.655)*	10004.185 (83.2)**
AUC_{extra}(%)	8.577 (67.979)*	8.857 (73.522)**
$t_{½\ el}$ (h)	2.47 (193.125)*	1.6 (25.455)**
k_{el} (1/h)	0.456 (39.548)*	0.47 (36.219)**
CL/F (L/h)	465.824 (91.461)*	489.389 (121.035)*
Vz/F (L)	1147.375 (67.318)*	1091.022 (110.983)*

*Values are geometric means (geometric CV%) for C_{max}, AUC_{0-6}, AUC_{0-t}, AUC_{0-inf}, CL/F and Vz/F, arithmetic mean (arithmetic CV%) for AUC_{extra}, $T_{1/2\ el}$ and k_{el} and median (min – max) for T_{max}; *n=36; **n=38*

Results of the statistical analysis showed that differences between the standardized and non-standardized uses in CBD C_{max}, T_{max}, AUC_{0-t}, AUC_{0-inf}, k_{el} and $T_{1/2\ el}$ were not statistically significant ($p \geq 0.2644$).

Secondary PK endpoints:

Peak concentrations of CBD metabolites were achieved approximately at 10 min (7-OH-CBD) and 30 min (7-COOH) post-dose, which is approximately 4 mins and 24 mins later than for the parent compound, respectively, for both product uses.

THC and in particular its metabolites plasma concentrations were quite low compared to CBD.

Adverse events

No SAEs, AESIs, AEs indicating abuse potential or other significant AEs occurred during the study and no participant discontinued from the study due to an AE.

Four (4) TEAEs were experienced by 3 (7.5%) participants overall. All TEAEs were deemed related to study treatment by the investigator and resolved by study end.

All reported TEAEs were either of mild or moderate intensity. No severe TEAE occurred.

The most frequent TEAE was cough: 2 cough events were reported for 2 participants (1 event each) during the non-standardized product use. In addition, vomiting and headache were both experienced by a different participant during standardized administration. No cough TEAE were recorded with the standardized product use.

The overview of TEAEs is presented in the following table:

Category	**Standardized use N=40**		**Non-standardized use N=40**		**Overall N=40**	
	n AE	**n (%)**	**n AE**	**n (%)**	**n AE**	**n (%)**
All TEAEs	2	1 (2.5)	2	2 (5.0)	4	3 (7.5)
AESI	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
AE indicating abuse potential	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Related	2	1 (2.5)	2	2 (5.0)	4	3 (7.5)
Not related	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
Leading to discontinuation	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
SAEs	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)

The number (n) and the proportion of participants with any adverse event and the number of adverse events (n AE) for each classification level are reported.

The overview of TEAEs intensity is presented in the following table:

Category	**Standardized use N=40**		**Non-standardized use N=40**		**Overall N=40**	
	N AE	**n (%)**	**N AE**	**n (%)**	**N AE**	**n (%)**
All TEAEs	2	1 (2.5)	2	2 (5.0)	4	3 (7.5)
Mild	1	1 (2.5)	1	1 (2.5)	2	2 (5.0)
Moderate	1	1 (2.5)	1	1 (2.5)	2	2 (5.0)
Severe	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)

Number of TEAEs and number of participants with TEAEs by System Organ Class (SOC), preferred term (PT) and product use is presented in the following table:

System Organ Class	**Standardized Use N=40**		**Non-standardized Use N=40**		**Overall N=40**	
Preferred term	**N AEs**	**n (%) Subj**	**N AEs**	**n (%) Subj**	**N AEs**	**n (%) Subj**
All TEAEs – all SOCs	2	1 (2.5)	2	2 (5.0)	4	3 (7.5)
Respiratory, thoracic and mediastinal disorders	0	0 (0.0)	2	2 (5.0)	2	2 (5.0)
Cough	0	0 (0.0)	2	2 (5.0)	2	2 (5.0)
Gastrointestinal disorders	1	1 (2.5)	0	0 (0.0)	1	1 (2.5)
Vomiting	1	1 (2.5)	0	0 (0.0)	1	1 (2.5)
Nervous system disorders	1	1 (2.5)	0	0 (0.0)	1	1 (2.5)
Headache	1	1 (2.5)	0	0 (0.0)	1	1 (2.5)

MedDRA version 28.0

No clinically relevant changes in vital signs, body weight, ECG, spirometry results, physical examination findings or safety laboratory parameters occurred. No clinically significant respiratory test parameters were observed.